

Remarks

Reconsideration of this Application is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 103

In the Office Action dated March 24, 2005, claims 27, 31, 36, 39, 120, 124, 128 and 130 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Savage, WO 99/64464 (hereinafter "Savage"); in view of Cormier *et al.*, *Int. J. Cancer* 75:517-524 (1998) (hereinafter "Cormier"); Schnell *et al.*, *J. Immunol.* 164:1243-1250 (2000) (hereinafter "Schnell"); and Zarour *et al.*, *Proc. Natl. Acad. Sci. USA* 97:400-405 (2000) (hereinafter "Zarour"). Applicants respectfully traverse this rejection.

The Office Action stated that

One would have been motivated with a reasonable expectation of success to create an MHC/antibody compound as taught by Savage to increase the presentation of antigenic peptides on the surface of the tumor cell. The artisan would have been further motivated to use a MelanA/MART antigenic peptide as the target because Cormier teaches that it is present in a majority of melanomas and because there may be down-regulation of MAA in tumor cells to escape immune recognition. The artisan would have been further motivated with a reasonable expectation of success to, based on the teachings of Savage regarding the class I/antibody constructs, to also make class II/antibody constructs based on the teachings of Schnell that T cell help (a class II driven event) augments the cytotoxic T cell response (a class I driven event) to tumors and the teachings of Zarour that no significant class I CD8+T cell response were [sic] observed in patients in the absence of detectable class II CD4+ T cell response to MelanA/MART

March 24, 2005 Office Action, p. 3. (citation omitted).

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103, the prior art must teach or suggest all the limitations of the claims. There must also be some suggestion or motivation to combine the teachings or modify the prior art to arrive at the claimed invention. Finally, the teaching or suggestion to modify the prior art must come from the prior art itself and not the application. *See In re Vaeck*, 20 U.S.P.Q.2d (BNA) 1438 (Fed. Cir. 1991).

First, the references described by the examiner do not in themselves provide a motivation to combine or modify their teachings. Second, while the examiner has attempted to provide a line of reasoning as to why a skilled artisan would have found the invention obvious in light of the references cited, the examiner has not put his knowledge of the applicant's disclosure aside and stepped back in time to just before the invention was made. Rather, the examiner has improperly relied upon hindsight reasoning, based on the applicant's disclosure, in combining the cited references in support of the rejection under 35 U.S.C. § 103(a). *Cf.* M.P.E.P. §§ 2142 and 2143 (rev. 2 8th ed. May 2004).

Savage teaches an MHC class I - antibody complex, but does not teach or suggest an MHC class II - antibody complex. Further, as the examiner points out, nothing in Savage teaches nor suggests the melanoma antigen of the claims. Moreover, nothing in Savage teaches nor suggests linking an MHC complex with a melanoma antigen to an antibody or fragment thereof with and antibody specific for the cell surface marker CEA.

Schnell only discloses that dendritic cells (DCs) genetically modified to express both MHC class I and class II epitopes induce more effective tumor immunity than DCs expressing only MHC class I. Nothing in Schnell teaches or suggests making MHC-peptide complexes, much less MHC-peptide complexes linked to an antibody, because

only the antigenic peptides are used. Further, the antigenic peptides are transduced into dendritic cells, not targeted to tumor cells as is the presently claimed invention. Further, Schnell gives no indication that MHC class II peptides alone would induce more effective tumor immunity. Rather, Schnell teaches that both MHC class I and class II peptides are required. In fact, according to Schnell, "our findings . . . underline the need to combine class I and class II epitopes appropriately to maximize the effectiveness of adoptively transferred DCs." *See* p. 1243. Thus, Schnell describes a need to combine MHC class I and class II peptides, not a need to create MHC class II-peptide complexes linked to an antibody.

In addition, a skilled artisan reading Savage and Schnell would not be motivated to produce an MHC- MelanA/MART antigenic peptide complex linked to an antibody specific for the cell surface marker. First, there is no motivation provided within either Savage or Schnell to combine the teachings of the references. Second, even if a motivation to combine the teachings of Savage and Schnell existed, as the examiner points out, the combination of Savage and Schnell does not teach the melanoma antigen of the claims. Thus, one would not be motivated, from the disclosures of Savage and Schnell, to arrive at the claimed invention.

Further, there is no motivation within any of Savage, Schnell, Cormier or Zarour to combine the teachings of these four references. Moreover, even if such a motivation did exist, Zarour and Cormier do not cure the deficiencies of the teachings of Savage and Schnell.

While Cormier may teach that tumor-infiltrating lymphocytes can recognize MelanA/MART in the context of MHC class I presentation, Cormier does not provide

any indication that tumor-infiltrating lymphocytes can recognize MelanA/MART in the context of MHC class II presentation and further provides no motivation or suggestion to investigate that possibility. In fact, Cormier does not mention class II MHC molecules, nor describe their involvement in tumor immunity. Nothing in Cormier teaches nor suggests modifying the disclosures of Savage or Schnell to arrive at the claimed invention.

Zarour is directed to the identification of a class II MHC epitope encoded by the MelanA/MART-1 gene. The examiner notes that Zarour teaches that no significant class I CD8+ T cell response was observed in the absence of a detectable class II CD4+ T cell response to MelanA/Mart-1. However, this leads the authors to suggest "vaccination with protein or multivalent peptides including class-I and class-II restricted epitopes . . . in patients with melanoma" Zarour at page 405. Nothing in Zarour teaches anything other than using the proteins or peptides themselves as cancer vaccines. There is nothing in Zarour to suggest linking an MHC class II complex which includes a MelanA/MART antigen to an antibody specific for the cell marker CEA.

Therefore, while Savage teaches certain class I MHC - antibody complexes, nothing in Savage suggests class II MHC - antibody complexes. Further, nothing in Schnell, Cormier or Zarour suggests modifying Savage to arrive at the presently claimed invention. Specifically, nothing in Schnell, Cormier or Zarour provides a motivation to modify Savage to make an MHC class II complex which includes a MelanA/MART antigen coupled to an antibody specific for the cell marker CEA.

Accordingly, a *prima facie* case of obviousness has not been established.

Withdrawal of this rejection is respectfully requested.

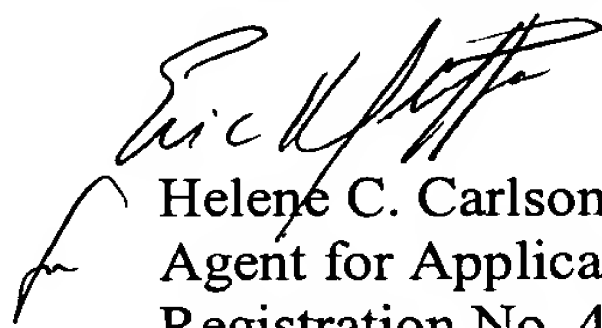
Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

 36,688
Helene C. Carlson
Agent for Applicants
Registration No. 47,473

Date: September 26, 2005

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
434510_1.DOC